Amendments to the Claims:

The following listing reflects amendments to the claims and replaces all prior versions and listings of claims in this application.

1-104. (Canceled).

105. (Currently Amended) A conjugate formed by reaction of an active agent comprising a reactive thiol group with a water-soluble polymer having the structure:

wherein:

POLY is a water-soluble polymer segment.

b is 0 or 1.

X is a hydrolytically stable linker comprising at least 4 contiguous saturated carbon atoms <u>adjacent to the nitrogen atom of the maleimide ring</u>, and said polymer is absent aromatic groups and ester linkages.

106. (Currently Amended) A conjugate comprising the following structure:

wherein:

POLY is a water-soluble polymer segment,

b is 0 or 1.

X is a hydrolytically stable linker comprising at least 4 contiguous saturated carbon atoms adjacent to the ring nitrogen atom.

"POLY-[O] $_{b}$ -C(O)-NH-X-" is absent aromatic groups and ester linkages, and

"-S-active agent" represents a residue of an active agent comprising a thiol (-SH) group.

107. (Original) A composition comprising the conjugate of claim 106, wherein said composition comprises a single polymer conjugate species.

108-130. (Canceled)

- 131. (Previously Presented) The conjugate of claim 105, wherein said active agent is selected from the group consisting of small molecules, peptides, and proteins.
- 132. (Previously Presented) The conjugate of claim 106, wherein said active agent is selected from the group consisting of small molecules, peptides, and proteins.
- 133. (Previously Presented) The conjugate of claim 106, wherein POLY is selected from the group consisting of poly(alkylene oxide), poly(vinyl pyrrolidone), poly(vinyl alcohol), polyoxazoline, poly(acryloylmorpholine), and poly(oxyethylated polyol).
- 134. (Previously Presented) The conjugate of claim 133, wherein POLY is a poly(alkylene oxide).
- 135. (Previously Presented) The conjugate of claim 134, wherein POLY is a poly(ethylene glycol).

136. (Previously Presented) The conjugate of claim 135, wherein the poly(ethylene glycol) is terminally capped with an end-capping moiety.

- 137. (Previously Presented) The conjugate of claim 136, wherein the end-capping moiety is selected from the group consisting alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, alkynyloxy, substituted alkynyloxy, aryloxy, and substituted aryloxy.
- 138. (Previously Presented) The conjugate of claim 137, wherein the end-capping moiety is selected from the group consisting of methoxy, ethoxy, and benzyloxy.
- 139. (Previously Presented) The conjugate of claim 135, wherein the poly(ethylene glycol) has a nominal average molecular mass of from about 100 daltons to about 100,000 daltons.
- 140. (Previously Presented) The conjugate of claim 139, wherein the poly(ethylene glycol) has a nominal average molecular mass of from about 1,000 daltons to about 50,000 daltons.
- 141. (Previously Presented) The conjugate of claim 140, wherein the poly(ethylene glycol) has a nominal average molecular mass of from about 2,000 daltons to about 30,000 daltons.
- 142. (Previously Presented) The conjugate of claim 135, wherein said poly(ethylene glycol) has a structure selected from the group consisting of linear, branched and forked.

143. (Previously Presented) The conjugate of claim 142, wherein said poly(ethylene glycol) comprises the structure:

Z-(CH2CH2O)n-CH2CH2-.

where n is from about 10 to about 4000, and Z comprises a moiety selected from the group consisting of hydroxy, amino, ester, carbonate, aldehyde, aldehyde hydrate, acetal, ketone, ketone hydrate, ketal, alkenyl, acrylate, methacrylate, acrylamide, sulfone, thiol, carboxylic acid, isocyanate, isothiocyanate, hydrazide, urea, maleimide, vinylsulfone, dithiopyridine, vinylpyridine, iodoacetamide, alkoxy, benzyloxy, silane, lipid, phospholipid, biotin, and fluorescein.

- 144. (Previously Presented) The conjugate of claim 135, wherein X is a saturated acyclic, cyclic, or alicyclic hydrocarbon chain having a total number of carbon atoms selected from the group consisting of 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, and 20.
- 145. (Currently Amended) The conjugate of claim 144, wherein X is a saturated acyclic, cyclic, or alicyclic hydrocarbon chain having a total number of carbon atoms selected from the group consisting of: from about 4 to about 12, from about 4 to about 10, and from about 5 to about 8 atoms.
- 146. (Previously Presented) The conjugate of claim 135, wherein X is a linear saturated acyclic hydrocarbon chain.
- 147. (Previously Presented) The conjugate of claim 135, wherein X is a branched saturated acyclic hydrocarbon chain.
- 148. (Previously Presented) The conjugate of claim 147, wherein X is branched at the carbon α to the maleimidyl group.

149. (Previously Presented) The conjugate of claim 147, wherein X is branched at the carbon β to the maleimidyl group.

150. (Previously Presented) The conjugate of claim 147, wherein X is branched at the carbon y to the maleimidyl group.

151. (Previously Presented) The conjugate of claim 146, having the structure:

$$POLY-[O]_b-C-NH-\begin{bmatrix}R^1\\C\\R^2\end{bmatrix}_y$$
 active agent

wherein:

y is an integer from 4 to about 20:

R¹, in each occurrence, is independently H or an organic radical that is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl, and

R², in each occurrence, is independently H or an organic radical that is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl.

152. (Previously Presented) The conjugate of claim 151, wherein either (i) R^1 and R^2 in each occurrence is independently H or an organic radical selected from the group consisting of lower alkyl and lower cycloalkyl or (ii) R^1 and R^2 are both H, and y is selected from the group consisting of 4, 5, 6, 7, 8, 9, and 10.

153. (Previously Presented) The conjugate of claim 151 having the structure:

$$\begin{array}{c|c} \text{POLY-[O]}_b\text{-C} - \text{NH} & \begin{array}{c|c} R^1 & R^1 \\ C & C \\ R^2 & R^2 \end{array} \\ \begin{array}{c} \text{active agent} \\ \text{y-1} \end{array}$$

wherein at least one of R^1 or R^2 on C_α is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl.

154. (Previously Presented) The conjugate of claim 153, wherein each of R^1 and R^2 on C_α is independently selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl.

155. (Previously Presented) The conjugate of claim 153, wherein all other non- $C_{\alpha}R^{1}$ and R^{2} variables are H.

156. (Previously Presented) The conjugate of claim 153 wherein at least one of R^1 or R^2 on C_α is lower alkyl or lower cycloalkyl.

157. (Previously Presented) The conjugate of claim 153, wherein R² on C_a is H.

158. (Previously Presented) The conjugate of claim 157, wherein R^1 on C_{α} is selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, pentyl, cyclopentyl, hexyl, and cyclohexyl.

159. (Previously Presented) The conjugate of claim 153 having the structure:

$$\begin{array}{c|c} O & & & \\ O & & & \\ POLY-[O]_b-C-NH- & & & \\ C & & & & \\ H & & & \\ R^2 & & & \\ Y-I & & & \\ \end{array}$$

wherein R¹and R² are each independently alkyl or cycloalkyl.

160. (Previously Presented) The conjugate of claim 153, having the structure:

$$POLY-[O]_b-C-NH = \begin{bmatrix} H \\ I \\ C \\ I \\ R^2 \end{bmatrix} \begin{bmatrix} R^1 \\ R^2 \\ S \end{bmatrix}$$
 active agent

wherein R1 is alkyl or cycloalkyl and R2 is H.

- 161. (Previously Presented) The conjugate of claim 159 wherein R^1 and R^2 are each independently either methyl or ethyl.
- 162. (Previously Presented) The conjugate of claim 159, wherein $\ensuremath{\mathsf{R}}^1$ and $\ensuremath{\mathsf{R}}^2$ are the same.
- 163. (Previously Presented) The conjugate of claim 149 having the structure:

wherein R¹and R² are each independently selected from the group consisting of H, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl, but are not both H.

164. (Previously Presented) The conjugate of claim 163, wherein R¹ and R² are each independently H, lower alkyl or lower cycloalkyl.

165. (Previously Presented) The conjugate of claim 164, wherein R¹ and R² are each independently selected from the group consisting of H, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, pentyl, cyclopentyl, hexyl, and cyclohexyl.

166. (Previously Presented) The conjugate of claim 163, wherein R² is H.

167. (Previously Presented) The conjugate of claim 151, having the structure:

$$POLY-[O]_b - C - NH \longrightarrow \begin{bmatrix} R_1 \\ C \\ L \\ R_2 \end{bmatrix} \begin{bmatrix} R_1 & R_1 & R_1 \\ C \\ R_2 & R^2 \end{bmatrix} \begin{bmatrix} R_1 & R_1 \\ C \\ R_2 & R_2 \end{bmatrix}$$
 active agent

wherein at least one of R^1 and R^2 attached to C_γ is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl.

168. (Previously Presented) The conjugate of claim 167, wherein at least one of R¹ and R² attached to C, is alkyl or cycloalkyl and all other R¹ and R² variables are H.

169. (Previously Presented) The conjugate of claim 167, wherein one of the R^1 variables attached to C_α or C_β is alkyl or cycloalkyl, and all other R^1 and R^2 variables are H.

170. (Previously Presented) The conjugate of claim 106, wherein X is a saturated cyclic or alicyclic hydrocarbon chain.

171. (Previously Presented) The conjugate of claim 170, wherein X has the structure:

$$\begin{bmatrix} R^1 \\ C \\ R^2 \end{bmatrix}_q CYC_a \begin{bmatrix} R^1 \\ C \\ R^2 \end{bmatrix}_{p_1}$$

and

 \mbox{CYC}_a is a cycloalkylene group having "a" ring carbons, where the value of "a" ranges from 3 to 12;

p and q are each independently 0 to 20, and p +q + a < 20.

R¹, in each occurrence, is independently H or an organic radical that is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl, and

R², in each occurrence, is independently H or an organic radical that is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl.

- 172. (Previously Presented) The conjugate of claim 171, wherein p and q are each independently selected from the group consisting of 0, 1, 2, 3, 4, 5, 6, 7, and 8.
- 173. (Previously Presented) The conjugate of claim 171, wherein R¹, in each occurrence, is independently H or an organic radical that is either lower alkyl or lower cycloalkyl, and R², in each occurrence, is independently H or an organic radical that is either lower alkyl or lower cycloalkyl.
- 174. (Previously Presented) The conjugate of claim 171, wherein a is selected from the group consisting of 5, 6, 7, 8 and 9.

175. (Previously Presented) The conjugate of claim 174, wherein a is 6 and CYC_a is a 1.1-, 1.2-, 1.3- or 1.4-substituted cyclohexyl ring.

176. (Previously Presented) The conjugate of claim 171, wherein p and q each independently range from 0 to 4.

177. (Previously Presented) The conjugate of claim 175, wherein the substituents on said substituted cyclohexyl ring are *cis*.

178. (Previously Presented) The conjugate of claim 175, wherein the substituents on said substituted cyclohexyl ring are *trans*.

179. (Previously Presented) The conjugate of claim 171, wherein R^1 and R^2 are H in every occurrence.

180. (Previously Presented) The conjugate of claim 173, having the structure:

$$\text{POLY-[O]}_{b}\text{-C-NH-}(\text{CH}_{2})_{q}\text{--NH-}(\text{CH}_{2})_{q}\text{--NH-}(\text{CH}_{2})_{p}\text{--NH-}(\text{CH}_{2})_{p}\text{--NH-}(\text{CH}_{2})_{q}\text{--$$

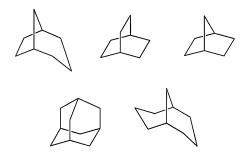
wherein q and p each independently range from 0 to 6.

181. (Previously Presented) The conjugate of claim 180, wherein q ranges from 0 to 6 and p is zero.

182. (Previously Presented) The conjugate of claim 173, having the structure:

wherein q and p each independently range from 0 to 3, and the substituents on the cyclohexylene ring are either cis or trans.

- 183. (Previously Presented) The conjugate of claim 171, wherein CYC_a is bicyclic or tricyclic.
- 184. (Previously Presented) The conjugate of claim 183, wherein CYC_a is selected from the group consisting of:



and said ring substituents are positioned at any available position on the bi or tricyclic ring.

185. (Currently Amended) The conjugate of claim 106 having the structure:

wherein X and b are as previously defined.

b' is 0 or 1, and

X' is a hydrolytically stable linker comprising at least 4 contiguous saturated carbon atoms adjacent to the ring nitrogen atom.

186. (Previously Presented) The conjugate of claim 106, corresponding to the structure:

wherein:

d is an integer from 3 to about 100, and

R is a residue of a central core molecule having 3 or more hydroxyl groups, amino groups, or combinations thereof.

187. (Previously Presented) The conjugate of claim 186, wherein d is an integer from 3 to about 12.

Application No. 10/751,274

188. (Previously Presented) The conjugate of claim 105, wherein POLY is a multi-arm polymer segment, and said polymer corresponds to the structure:

where

PEG is -(CH2CH2O)nCH2CH2-,

M is:

and m is selected from the group consisting of 3, 4, 5, 6, 7, and 8.